UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/382,242	08/24/1999	DAN E. ROBERTSON	DIVER1180-1	4972

25225 7590 09/21/2004

MORRISON & FOERSTER LLP
3811 VALLEY CENTRE DRIVE
SUITE 500
SAN DIEGO, CA 92130-2332

EXAMINER	
PROUTY, REBECCA E	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/382,242	ROBERTSON ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,26-29,31-35,38-42 and 44-56* is/are pending in the application.

4a) Of the above claim(s) *51* is/are withdrawn from consideration.

5)☒ Claim(s) *21,44,46 and 47* is/are allowed.

6)☒ Claim(s) *26-29,32-35,38-42,45,48-50 and 52-56* is/are rejected.

7)☒ Claim(s) *31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/9/04 has been entered.

Claims 1-20, 22-25, 30, 36, 37, and 43 have been canceled. Claims 21, 26-29, 31-35, 38-42, 44-53 and newly presented claims 54-56 are still at issue and are present for examination.

Applicants' arguments filed on 7/9/04, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim 51 remains withdrawn from consideration as being directed to a non-elected invention.

Claim 31 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 21. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in

wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 27-29, 32, 33, 35, 38-42, 48-50, and 52-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33 and 41 are indefinite in the recitation of "the oligonucleotide probe of claim 32 (or 40)" as claims 32 and 40 recite a composition.

Claims 27, 35, 48, and 54 (upon which Claims 28, 29, 32, 33, 38-42, 49, 50, 52, 53, 55 and 56 depend) is indefinite in the recitation of "specifically hybridizes to a nucleic acid having 90% (or 95%) identity to SEQ ID NO:23" as it is unclear how a nucleic acid can specifically hybridize to more than one nucleic acid sequence as specifically hybridize in the art means binds to a particular nucleic acid sequence but not to other different sequences.

Claims 26-28, 32-35, 38-42, 45, 48-50, and 52-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in

such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 26-28, 32-35, 38-42, 45, 48-50, and 52-56 are directed to a genus of oligonucleotide probes which comprise/consist of a sequence which specifically hybridizes to SEQ ID NO:23, its complement or to a nucleic acid having 90% or 95% identity thereto which encodes an esterase.

The specification does not contain any disclosure of the structure and function of all oligonucleotide probes which comprise/consist of a sequence which hybridizes to SEQ ID NO:23, its complement or to a nucleic acid having 90% or 95% identity thereto. The genus of probes that comprise a sequence which specifically hybridizes to SEQ ID NO:23, its complement or to a nucleic acid having 95% identity thereto is a large variable genus with the potentiality of encoding many different proteins. Therefore, many structurally and functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only SEQ ID NO:23 which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot

reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Applicants argue that the claimed probes are described by features analogous to those found in example 9 of the written description guidelines. However, the instant claims are not analogous to those of example 9. The claim recited in example 9 is limited to a genus of nucleic acids which all have the same function (i.e., encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity) while applicants claims are not as has been repeatedly noted in previous Office Actions. Significantly the claim of example 9 does not read "An isolated nucleic acid (or An oligonucleotide probe) that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO: 1." nor do applicants claims read "An oligonucleotide probe that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO:23 wherein said oligonucleotide probe encodes a protein having

esterase activity." Applicants state that Example 9 is silent with regard to the number and percentage of sequences that did not encode proteins having activity similar to SEQ ED NO:1. While this is true, in Example 9, **these sequences are not claimed** while in the instant situation applicants claims encompass such sequences. Applicants argue that the Guidelines indicate that importation of specific hybridization conditions into the claim text is not required to meet the written description requirements. However, applicants have never been required to import specific hybridization conditions into the claim text to meet the written description requirements. In the instant application importation of specific hybridization conditions into the claims was necessary to meet the definiteness requirements of 112, 2nd paragraph and **not** in order to meet the written description requirement. Finally, applicants argue "The highly stringent conditions of Example 9 are sufficiently analogous to the stringent conditions of the instant claimed invention such that a person of skill in the art would not expect substantial variation among species encompassed within the scope of the instant claims because the claimed stringent conditions yield structurally similar DNAs". However, it is noted that the two situations are not in fact nearly so

similar because in Example 9 of the guidelines "highly stringent conditions" are defined as 6XSSC and 65 degrees Celsius while in the instant claims the conditions recited are 45°C in 0.9 M NaCl, 50 mM NaH_2PO_4, pH 7.0, 5.0 mM Na_2EDTA, 0.5% SDS, 10X Denhardt's and 0.5 mg/ml polyriboadenylic acid and a wash step comprising 30 minutes at room temperature in a buffer comprising 150 mM NaCl, 20 mM Tris hydrochloride, pH 7.8, 1 mM Na_2EDTA, 0.5% SDS. followed by a 30 minute wash in the buffer. While the conditions recited in Example 9 are highly stringent, applicants recited conditions are very low stringency and thus will allow much more variation even in the recited structural features of the claims than is present within the claim of Example 9 of the guidelines. For all the above reasons applicants claims are not analogous to those of Example 9 of the guidelines, and lack sufficient written description for all the reasons previously discussed.

Claims 26-28, 32-35, 38-42, 45, 48-50, and 52-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a probe consisting of a fragment of SEQ ID NO:23 which will hybridize to SEQ ID NO:23 under stringent conditions and optionally a detectable label, does not reasonably provide enablement for any probe which

hybridizes to any nucleic acid having 90% or 95% identity to SEQ ID NO:23 under the recited conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 27, 35, 48, and 54 (and Claims 28, 32, 33, 38-42, 49, 50, 52, 53, 55 and 56 which depend therefrom) are so broad as to encompass any probe which comprises/consists of a nucleic acid which specifically hybridizes to any nucleic acid having 95% or 90% identity to SEQ ID NO:23 at 45°C in 0.9 M NaCl, 50 mM NaH_2PO_4, pH 7.0, 5.0 mM Na_2EDTA, 0.5% SDS, 10X Denhardt's and 0.5 mg/ml polyriboadenylic acid and a wash step comprising 30 minutes at room temperature in a buffer comprising 150 mM NaCl, 20 mM Tris hydrochloride, pH 7.8, 1 mM Na_2EDTA, 0.5% SDS. followed by a 30 minute wash in the buffer while Claims 26 and 34 encompasses any probe which comprises/consists of a nucleic acid which specifically hybridizes to SEQ ID NO:23 under these conditions. The specification teaches a use of only probes which will specifically hybridize to SEQ ID NO:23 (to identify organisms having esterase function) as the specification has not identified any use for the vast number of nucleic acids having 90% or 95% identity thereto. Only a very small number of such

polynucleotides will encode esterase proteins and the positions within a sequence where modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. Furthermore, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. Thus one of skill in the art would not know which of the vast numbers of sequences having 90% or 95% identity to SEQ ID NO:23 would be useful, such that probes which would specifically hybridize thereto would be useful. Furthermore, designing probes which would specifically detect any particular sequence under the recited conditions would require undue experimentation as under the recited low stringency conditions this would likely be impossible while under higher stringencies the structural requirements of the probe would vary depending on not only the hybridization conditions to be used but also the type of material to be

tested. Without knowledge of what nucleic acids must be distinguished from the target of interest may be present in the material to be tested one of skill in the art could not determine number of mismatches to the target sequence a probe could have and still hybridize specifically to the target sequence. As such it is highly unpredictable whether a probe which will specifically hybridize to any particular target can be made and it would require undue experimentation to make and use the entire scope of the claimed probes. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of DNAs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants argue that the Patent Office remains concerned that because the claims allegedly recite low stringency hybridization conditions, it would take undue experimentation to use most of the claimed probes as asserted in the specification. To address these concerns, the Applicants have amended the appropriate claims to add the limitation that the probes

hybridize under "stringent conditions" (as expressly defined by the specification) to nucleic acids encoding a polypeptide having esterase activity. However, it is noted that applicants amendments have not addressed the problem delineated by the previous Office Action. The term "stringent conditions" in no way limits the claims the high stringency conditions and in view of the recited conditions the claims clearly still encompass conditions which are of very low stringency.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26-28, 48-49, and 52-53 are rejected under 35 U.S.C. 102(a or b) as being anticipated by GenBank Accession No. X86487 or Kim et al.

GenBank Accession No. X86487 and Kim et al. each teach the isolation of a gene having a nucleotide sequence comprising at least 15 nucleotides of the nucleotide sequence of SEQ ID NO:23. Bases 21-39 of the gene of GenBank Accession No. X86487 are identical to bases 360-378 of SEQ ID NO:23 and bases 5051-5069

of the gene of Kim et al. are identical to bases 505-523 of SEQ ID NO:23. As bases 21-39 of the sequence of GenBank Accession No. X86487 are 100% identical to bases 360-378 of SEQ ID NO:23 and bases 5051-5069 of the gene of Kim et al. are 100% identical to bases 505-523 of SEQ ID NO:23, each of these fragments would unquestionably specifically hybridize to SEQ ID NO:23 and the nucleic acids of GenBank Accession No. X86487 and Kim et al. each clearly comprise these fragments.

Applicants argue that the hybridization and length limitations of the instant claims, clearly differentiate the instant claims from the cited references. This is not persuasive because these limitations are met by the nucleic acids of the cited references. Claim 26 (the narrowest of the rejected independent claims) recites "An oligonucleotide probe at least 30 nucleotides in length (the nucleic acids of GenBank Accession No. X86487 and Kim et al. are 385 bp and 14133 bp in length respectively) **comprising** a nucleic acid sequence which specifically hybridizes under stringent conditions to a nucleic acid sequence to SEQ ID NO:23 (this limitation is met by nucleotides 21-39 of the gene of GenBank Accession No. X86487 and nucleotides 5051-5069 of the gene of Kim et al. which by virtue of the 100% identity to a portion of SEQ ID NO:23 would

hybridize thereto even under much more stringent conditions than the low stringency conditions recited in these claims). Claims 27 and 48 differ from Claim 26 only in that the internal fragment of the probe must hybridize to a nucleic acid having at least 95% or 90% identity to SEQ ID NO:23 and encoding an esterase instead of to specifically SEQ ID NO:23. Since as noted nucleotides 21-39 of the gene of GenBank Accession No. X86487 and nucleotides 5051-5069 of the gene of Kim et al. have 100% identity to a portion of SEQ ID NO:23 they would hybridize to SEQ ID NO:23 which is clearly within the scope of a nucleic acid having at least 95% or 90% identity to SEQ ID NO:23.

Claims 21, 44, 46 and 47 are allowed. These claims are restricted oligonucleotides consisting of at least 30 (or 50) contiguous nucleotides of SEQ ID NO:23 or compostions thereof. The prior art does not teach teaches polynucleotides consisting of at least 30 consecutive bases of SEQ ID NO:23.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Rebecca Prouty
Primary Examiner
Art Unit 1652